PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

11/8

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2005/000308	28.01.2005	28.01.2004

International Patent Classification (IPC) or both national classification and IPC
G01N1/28, G01N27/447, C12Q1/68

Applicant
NORCHIP

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

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If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Smith-Hewitt, L

Telephone No. +49 89 2399-2995

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2005/000308

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2005/000308

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	32
	No:	Claims	1-31
Inventive step (IS)	Yes:	Claims	
	No:	Claims	32
Industrial applicability (IA)	Yes:	Claims	1-32
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

1. Re Item V.

1.1 Document US2002/0045246 (D1) discloses:
An integrated lab-on-a-chip diagnostic system (see [0098], [0099]; microfabrication techniques) for carrying out a sample preparation process on a fluid sample (in this case cell lysis, nucleic acid extraction and detection) containing cells and/or particles [0012].

1.1.1 Although in the disclosure of D1 the chip is integrated onto a cartridge, the wording of the present claim 1 does not exclude this possibility. There is no stipulation in the present wording of the claims, for example, that the entire diagnostic "system" is integrated on the lab-on-a-chip. Thus systems where only part of the diagnostic apparatus is integrated on the lab on a chip also fall under the present wording. This view is reinforced by the present description on p.8, 3rd paragraph, which states that only "some of the components of the system" need to be microfabricated and integrated on a common substrate.

1.1.2 The system of D1 further comprises (see in particular Fig. 2):
(a) an inlet for a fluid sample (103);
(b) a lysis unit for lysis of cells and/or particles contained in the fluid sample (107, 119);
(c) a nucleic acid extraction unit for extraction of nucleic acids from the cells and/or particles contained in the fluid sample (122);
(d) a reservoir containing a lysis fluid(109);
(e) a reservoir containing an eluent for removing nucleic acids collected in the nucleic acid extraction unit (127);
wherein the sample inlet is in fluid communication with the lysis unit,
wherein the lysis unit is in fluid communication with the nucleic acid extraction unit, a valve being present to control the flow of fluid therebetween;
wherein the reservoir containing the lysis fluid is in fluid communication with the lysis unit, and wherein the reservoir containing the eluent is in fluid communication with the nucleic acid extraction unit, a valve being present to control the flow of fluid therebetween.

1.1.3 The subject matter of the present claim 1 is thus anticipated by the disclosure D1. Claim 1 lacks novelty in the sense of Article 33(2) EPC.

1.1.4 Furthermore, the additional features of dependent claims 2-6, 8 and 12-17 are anticipated by the disclosure between paragraphs [0068] and [0205].

1.1.5 The disclosure of paragraph [0074], teaches that an air gap separating elution fluid and wash fluid is advantageous. As for example present claim 11 states that "the common reservoir comprises a conduit in fluid communication with the inlet and lysis unit", the additional subject matter of claims 9-11 appears to be anticipated by the arrangement of the feeding conduit to device (122). Claims 9-11 cannot therefore be considered to be novel in the sense of Article 33(2) PCT.

1.1.6 The subject matter of claims 19([0114]), 20-22 ([0133]-[0139]) and 23-31 [0068]-[0205] is also anticipated by the disclosure of D1.

1.1.7 The additional features of claim 32 are considered to be novel over the disclosure of D1. Nevertheless, in the light of the disclosure of [0074], the method of separating process fluids by air in the same chamber would appear to be trivial, especially in the light of the disclosure of paragraph [0074], which specifically teaches that "air gaps" between fluids are advantageous. Said claim is thus not considered to fulfil the requirements for inventive step under Article 33(3) PCT.

1.1.8 Even if the wording of the present claim 1 were amended to read that "the lysis unit, the nucleic acid extraction unit, the lysis fluid reservoir and the eluent reservoir were microfabricated and formed on a common substrate", this difference over D1 could not be considered to be inventive in the sense of Article 33(3) PCT, as exactly the same functionality would be present, and as techniques for further miniaturisation were well developed at the time of filing the present application (see also D3, US2003/0138941 A1).

1.2 Document US6544734B1 (D2); (col.1,l.39 - col.2,l.47 and col.3,l.3-col.6,l.8, Abstract and Figures 1, 3) also anticipates the subject matter of claims 1-8,17-19,22-25,26-30. This is based on the interpretation of the term "reservoir" (claim 1) to mean any storage device for the various fluids, again due to the broad definition "integrated lab-on-a-chip diagnostic system", not necessarily being a part of the chip per se.

1.3 Document D3 (Fig. 1 and 11A, 11B; paragraphs [0082]-[0087], [0095]-[0102], [0120]-[0121], [0149]-[0153], [0158]-[0198]) also anticipates the subject matter of claims 1-8, 12-17 and 22-30. In addition, silica beads/particles are well known in nucleic acid purifying processes (see DE 197 00 364 A1, p.2, l.25-57), thus the skilled person would find it

obvious to incorporate them as part of the sample preparation steps on the chip described by D3. Claims 19 and 20 are thus not considered to be inventive over a combination of the disclosures D3 and D4 (Article 33(3) PCT).

1.4 Document D5 (JOON-HO KIM ET AL, "A disposable DNA sample preparation microfluidic chip for nucleic acid probe assay", PROCEEDINGS OF THE IEEE 15TH. ANNUAL INTERNATIONAL CONFERENCE ON MICROELECTRO MECHANICAL SYSTEMS. MEMS 2002. LAS VEGAS, NV, JAN. 20 - 24, 2002, IEEE INTERNATIONAL MICRO ELECTRO MECHANICAL SYSTEMS CONFERENCE, NEW YORK, NY : IEEE, US, the whole document, especially p.133, col.2, l.2-14 and Fig.1, but more importantly Fig. 11, "Sample loading") also discloses the containment of elution solution and wash solution in the same tube separated by air gaps as a method of operating a DNA chip, and thus anticipates the subject matter of present claims 9-12. The additional features of claim 32 seem to be trivial in the light of D5.

1.5 It can also be argued that document D6 (WO00/62931, Figs., p.7,l.10-p.16,l.22 and p.36,l.28-p.40,l.10) represents very close state of the art. Said disclosure anticipates the subject matter of claims 1-8, 12-17 and 22-31. D6 even describes on chip storage chambers for lysis and eluent fluids.

2. It is not at present apparent which part of the application could serve as a basis of a modified independent claim. Any future amended set of claims should be accompanied by a letter in which the difference of the subject-matter of the modified claims vis-à-vis the state of the art (Article 33(2) PCT) and the significance thereof (Article 33(3) PCT) is described. In such a case and in order to expedite examination of the requirements of Article 34(2)(b), the basis for all amendments is to be clearly identified with reference to the original application as filed.

Re: Item VI

3. The applicants are made aware of document D7 (WO2004/096443 A1), having a priority earlier than the present application (priority of 25-04-2003, filed on 19-04-2004) but published after (on 11-11-2004). Said document could be relevant to novelty in the regional phase.

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International Patent Classification (IPC) or both national classification and IPC G01N1/28, G01N27/447, C12Q1/68	
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Name and mailing address of the ISA: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Smith-Hewitt, L Telephone No. +49 89 2399-2995

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